学校编码：10384　　分类号＿＿＿＿密级＿＿＿＿

学　　号：200425052　　UDC＿＿＿＿

厦门大学

硕 士 学 位 论 文

铁（III）试剂催化的乙酸炔丙酯亲核取代反应的新方法学研究

The Research of New Synthetic Methodologies of Fe（III）Catalyzed Nucleophilic Substitution of Propargylic Acetates

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论文提交日期：　2 0 0 7　年　　月

论文答辩日期：　2 0 0 7　年　　月

学位授予日期：　2 0 0 7　年　　月

答辩委员会主席：＿＿＿＿＿＿＿＿

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摘 要

合成许多烯丙基化产物的一种直接而可靠的方法就是在过渡金属催化下，烯丙醇衍生物和亲核试剂在烯丙基位上发生亲核取代反应。相比而言，文献报道的过渡金属催化的炔丙醇衍生物和亲核试剂在炔丙基位上发生的取代反应却很少。由于炔官能团可以灵活方便的转化为其它官能团，这使得炔丙基位取代反应在有机合成中占有重要位置。

在炔丙基位的取代反应中，Nicholas 反应已经作为一种有力手段而被广泛接受，但是这个方法却存在一些缺陷。例如需要化学当量的[$Co_2(CO)_8$]，而且从炔丙醇经炔丙基的复杂配合物阳离子[$Co_2(CO)_6$(propargyl)]$^+$得到炔丙基产物需要几步反应。近来一些过渡金属催化的炔丙基位取代反应也见诸报道。最近文献报道的采用钌过渡金属配合物催化的炔丙位取代反应（图 1）。许多诸如醇类、胺类、酰胺类和硫醇类等亲核试剂都适用于这个反应。然而，在这种方法中反应底物通常只限于那些带有末端炔基官能团的炔丙醇类。最近，Toste 小组和 Campagne 小组分别报道了铼催化[(dppm) $ReOCl_3$]和金催化[$NaAuCl_4 \cdot 2H_2O$]的炔丙醇类的亲核取代反应。然而这些催化剂比较特殊而且价格昂贵，不适合大规模使用。因此，发展一种通用有效，成本低廉，方便使用的催化剂来催化炔丙基位的取代反应就显得尤为重要。

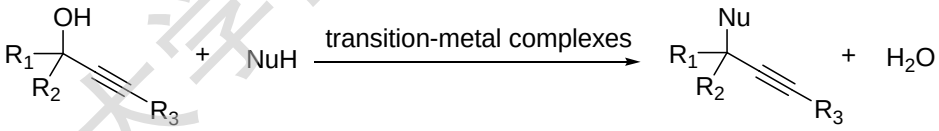


图 1. 过渡金属配合物催化的炔丙醇和各种亲核试剂的亲核取代反应

近来，铁化合物由于其毒性小，价格低以及对空气和少量水汽较不敏感的特性引起了化学家的注意。铁的电子排布是：[Fe]$3d^6 4s^2$。三价铁化合物表现出 Lewis 酸性，因此它们被应用于许多化学反应。其中，三氯化铁（$FeCl_3$）因为购买方便，价格低廉，性质稳定而尤其受到关注。

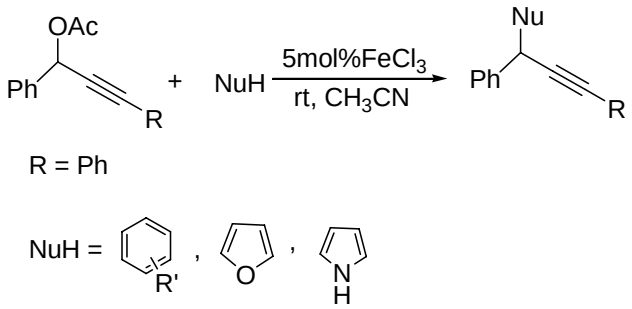


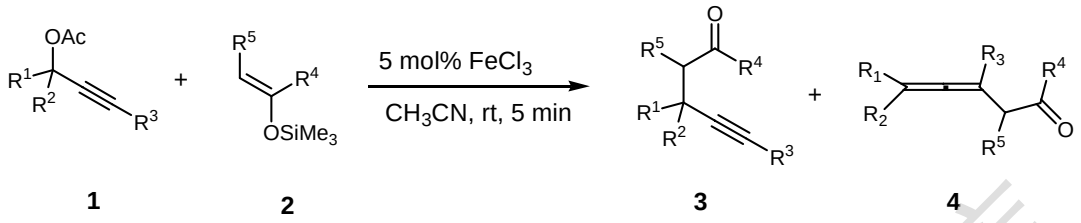
图 2　乙酸炔丙酯和芳香化合物在 $FeCl_3$ 催化下的取代反应

这里，我们发展了一种通用、高效的三氯化铁催化的乙酸炔丙酯与各种芳香化合物发生亲核取代反应的方法(图 2)。反应中的亲核试剂可以是苯类芳烃，呋喃和吡咯。反应导致 C-C 键的形成。具有末端炔基或非末端炔基的炔丙醇都容易进行反应。反应可以高产率、完全区域选择性的得到相应的炔丙基化产物。与通常用来催化炔丙醇亲核取代反应的钴、铼、钌、金的配合物相比较，用三氯化铁作为催化剂具有毒性较低、价格低廉、购买方便、反应条件温和等优点。因而这一方法能够作为以往传统方法的理想替代。

γ-炔酮是一类很有应用价值的有机中间体，是合成一系列呋喃，吡咯和噁唑的重要前体，在有机材料化学领域和药物化学领域它们的合成和反应一直是有机化学家关注的焦点。在形成γ-炔酮反应中，(1) 是通过共轭烯烃和炔烃或炔烃配合物的加成反应，用复杂的金属或者非金属络合物形成配体；(2) 是通过经典的炔丙醇亲核取代形成γ-炔酮，最近文献报道的多是采用一些过渡金属配合物催化炔丙醇亲核取代从而形成γ-炔酮。在这些报道当中，钌催化过程是一种通用而且直接的方法，成功的催化了炔丙醇和酮的亲核取代，然而，在这种方法中反应底物通常只限于那些带有末端炔基官能团的炔丙醇类。Teruaki Mukaiyama 和 Isamu Matsuda 分别报道了三苯甲基的高氯酸盐和复杂的 Ir 催化体系催化此过程，然而这些催化剂比较特殊而且价格昂贵，不适合大规模使用。有机酸催化被用来催化被他二羰基化合物与炔丙醇的亲核取代反应，从而得到γ-炔酮化合物。然而强酸性的反应环境同样使其应用并不乐观。因此，发展一种通用有效，成本低廉，方便使用的催化剂来高产率高效率的催化形成γ-炔酮就显得尤为重要。

我们实验室报道了一种用 Fe（III）试剂和 Bi(III)试剂为催化体系，高效的催化乙酸炔丙酯或炔丙醇和各种以杂原子或碳原子为中心的亲核试剂的亲核取代反应（图 3），在此基础上，我们

把这种体系拓展到形成γ-炔酮的反应方法上来（图 3）。



1　　2　　3　　4

图 3. 乙酸炔丙酯和烯醇硅醚在 $FeCl_3$ 催化下的取代反应

这里，我们发展了一种通用、高效的三氯化铁催化的乙酸炔丙酯与各种烯醇硅醚发生亲核取代反应得到γ-炔酮的方法。反应导致 sp^3-sp^3 C-C 键的形成。具有末端炔基或非末端炔基的乙酸炔丙酯都容易进行反应。反应可以高产率、较好区域选择性的得到相应的取代γ-炔酮产物。

发光材料广泛应用于通讯、卫星、雷达、显示、记录、光学、计算机、生物分子探针等高科技领域，因此目前对发光材料需求量很大。发光材料大体上可分为无机发光材料和有机发光材料两大类。与无机材料相比，有机材料具有更高的发光效率和更宽的发光颜色选择范围，并且具有容易大面积成膜的优越性。近年来，关于有机发光材料的研究愈来愈引起人们的兴趣。有机物发光领域包括光致发光、电致发光、化学发光、生物发光等。从分子结构上可将有机发光材料分为(1) 有机小分子(2) 有机高分子(3) 金属配合物，其中有机金属配合物也经常被归类在有机小分子之中。这些发光材料无论在发光机理,物理化学性能还是在应用上都有各自的特点,因而具有不同的应用前景。

1，3-二羰基化合物的烷基化是形成碳碳键的重要方法，通常该过程需要催化剂量的碱和有机卤代物作为烷基化试剂。另外一条途径是，在酸催化下，将亚甲基加成到醇上得到碳碳键。这条路径更具原子经济效益，也是现代有机合成的追求目标。在以往文献中，大多采用钌、铼 、汞 、金等化合物作为催化剂，不仅价格昂贵，毒性大，环境污染严重，而且催化效果一般，产率也一般。因此，发展一种通用有效，成本低廉，方便使用的催化剂来催化炔丙基位的取代反应就显得尤为重要。

这里，我们使用 $FeCl_3$/PTS（对甲基苯磺酸）催化成呋喃环反应（图 4），产物区域选择性高，适用于炔丙位碳为二级碳和三级碳的乙酸炔丙酯的反应，而且更加经济环保。同时在 PTS 的催化下，可以合成许多不同用途的中间体。

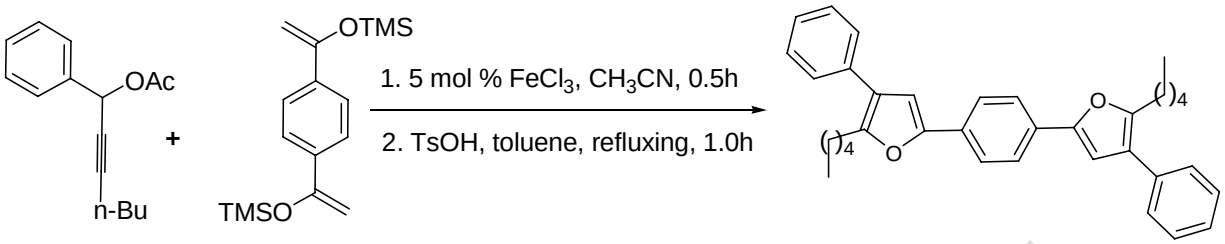


图 4 $FeCl_3$/PTS 催化成呋喃环反应

应用上述反应我们已经成功地制备了一系列单呋喃环的结构化合物，此次我们成功地将两个呋喃环连接在同一个苯环的对位上。我们对产物的光学性质做了简单测试，它在溶剂中呈现紫色荧光，有较高的量子产率。有很好的电子振动结构，最重要的是，该结构含有长的脂肪链，可以其在各种溶剂中的溶解度，这给应用于光电器材提供极大的便利。

关键词： 炔丙醇，三氯化铁，亲核取代； γ-炔酮，烯醇硅醚；光致发光，呋喃

Abstract

A direct and reliable approach to a wide variety of allylated products is the allylic substitution reaction of allylic alcohol derivatives with nucleophiles catalyzed by transition metal. In contrast, related transition metal–catalyzed propargylic substitution reaction of propargylic alcohol derivatives with nucleophiles are relatively rare. The flexibility of the alkyne functional group makes propargylic substitution reaction a pivotal role in organic synthesis.

The Nicholas reaction has been widely accepted as a powerful tool for propargylic substitution reaction but has some drawbacks: a stoichiometric amount of $[Co_2(CO)_8]$ is required, and several steps are necessary to obtain propargylic product from propargylic alcohols via cationic propargylic complexes $[Co_2(CO)_6(propargyl)]^+$. On the other hand, several transition metal-catalysed propargylic substitution reactions have been recently reported (Figure 1). Among them, a Ruthenium-catalysed process is a versatile and direct method. A wide variety of nucleophiles such as alcohols, amines, amides and thiols are available for this reaction. Nevertheless, with this method, the substrate is generally limited to the propargylic alcohols bearing terminal alkyne group. More recently, Toste and Campagne have described efficient rhenium [(dppm) $ReOCl_3$] and Gold [$NaAuCl_4 \cdot 2H_2O$] catalysed nucleophilic substitution of propargylic alcohols respectively. However, the specific and high cost of such catalysts makes a barrier to their large-scale use. Therefore, development of a general, efficient, cheap and readily available catalyst for propargylic substitution reaction is highly desirable.

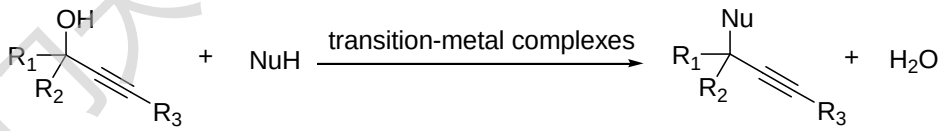


Figure 1. Nucleophilic Substitution Reactions of Propargylic Alcohols with Various Nucleophiles Catalyzed by Transition-Metal Complexes

Recently, Iron(III) compounds have received attention in organic synthesis due to their low toxicity, low cost and relative insensitivity to air and to small amounts of moisture. Iron(III) compounds exhibit Lewis acidity and they have been used in many chemical transformations. Iron trichloride is particularly attractive for us because it is commercially available and inexpensive, especially its stability.

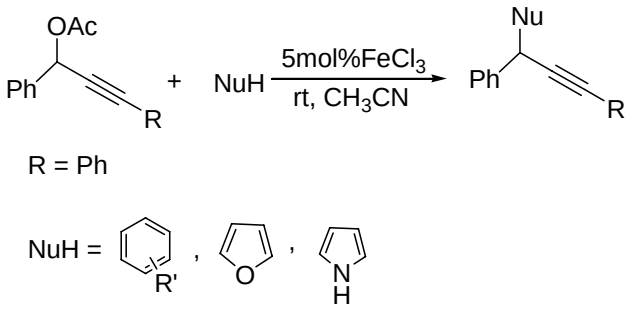


Figure 2. Nucleophilic Substitution Reactions of Propargylic acetates with Various aromatic compounds catalyzed by $FeCl_3$

Herein, we have developed a general and efficient $FeCl_3$-catalyzed substitution reaction of propargylic acetates with various aromatic compounds nucleophiles (Figure 2). The corresponding propargylic products were obtained in high yields with complete regioselectivity. In comparison with cobalt, rhenium, ruthenium and gold complexes, which are usually used to catalyse the nucleophilic substitution of propargylic alcohols, $FeCl_3$ as the catalyst offers several relevant advantages including cheapness and commercial availability, broad scope and mild reaction conditions of this transformation.

The acetylenic carbon-carbon triple bond plays a pivotal role in a variety of functional group transformations, which has resulted in the steady growth in the synthesis of propargylic derivatives. Unfortunately, the carbon-centered nucleophiles were limited to allyl silanes for the construction of sp^3-sp^3 C-C bonds in the reaction. Recently, Matsuda and co-workers reported that Iridium complex $[Ir(cod)\{P(OPh)_3\}_2]OTf$ serves as a catalyst for the transformation to γ-alkynyl ketones by the coupling of propargylic esters with enoxysilanes. Nishibayashi team also described an efficient coupling of propargylic alcohols with ketones for the formation of γ-alkynyl ketones in the presence of catalytic amount of a ruthenium catalyst. However, with this method, the propargylic alcohols bearing terminal alkyne group are the exclusive applicable substrate. Even so, the peculiarity and high cost of such catalysts make a barrier to their large-scale use. Therefore, development of a general, efficient, cheap and readily available catalyst for the formation of γ-alkynyl ketones by propargylic substitution reaction is of significance.

Recently, we have developed a highly efficient Iron(III) or Bismuth(III)-catalyzed propargylic substitution of propargylic alcohols or acetates with various heteroatom- and carbon-centered nucleophiles. Naturally we attempted to extend the scope of carbon-centered nucleophiles from allyl

silane to ketones or enoxysilanes for the formation of γ-alkynyl ketones. $FeCl_3$ as an efficient Lewis acid catalyst, has been widely used in many organic synthesis. So we employed $FeCl_3$ to catalyze the reaction of propargylic acetates with enoxysilanes (Figure 3).

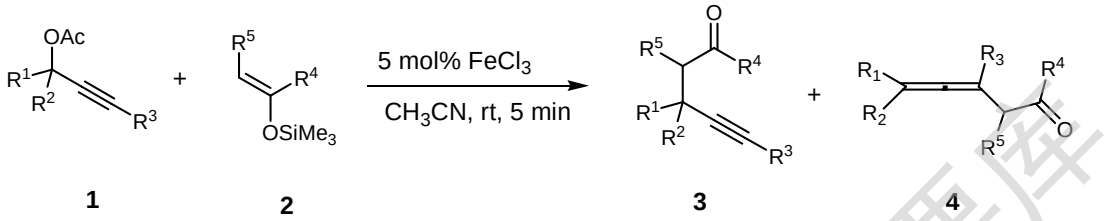


Figure 3 Nucleophilic Substitution Reactions of Propargylic acetates with enoxysilanes catalyzed by $FeCl_3$

Herein a novel and efficient procedure for the synthesis of γ-alkynyl ketones by the substitution reaction of propargylic acetates with enoxysilanes catalyzed by 5 mol % $FeCl_3$, has been developed. The reaction completed rapidly within very short time under mild conditions and air or moisture is tolerant. Propargylic acetates bearing terminal alkyne group or internal alkyne group are readily available. Such relevant advantages make our procedure an appealing alternative to current available methods to γ-alkynyl ketones.

Oligoaryl is an important class of compounds which exhibit a variety of fascinating properties for optoelectronic interests. Incorporation of five-membered heteroaromatic moieties into these conjugated molecules will occasionally increase fluorescence quantum yields and the optoelectronic properties of the oligomers can be tuned. Most syntheses of these heteroaromatic containing oligomers involve the transition-metal catalyzed cross coupling reactions of the corresponding aryl components. In general, the presence of a long chain aliphatic substituent in these heteroaromatic rings will increase the solubility in organic solvent and hence enhance the processibility of these materials. However, introduction of such alkyl substituent at C_3 and/or C_4 positions in these heteroaromatic rings for further cross coupling reactions is not trivial. Cyclization of the 1,4-dicarbonyl moiety with heteroatom-containing reagents provides an alternative procedure for the construction of these five-membered heterocycles. It is known that annulation of allenylmethanols can afford the corresponding five-membered oxygen heterocycles. In addition, annulation of allenyl carbonyl compounds propargylic acetals or oxiranes furnishes a powerful arsenal for the synthesis of substituted furans. The applications of propargylic metallic species have paved a useful path for the construction of furan skeletons.

We recently reported that the carbon-centered nucleophiles from allyl silane to ketones or enoxysilanes for the formation of γ-alkynyl ketones. $FeCl_3$ as an efficient Lewis acid catalyst, has been widely used in many organic synthesis. So we employed $FeCl_3$ to catalyze the reaction of propargylic acetates with enoxysilanes to achieve the formation of oligomers (Figure 4).

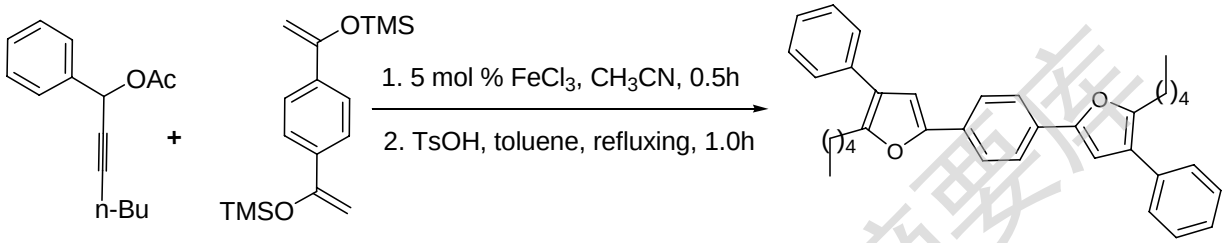


Figure 4 Nucleophilic Substitution Reactions of Propargylic acetates with enoxysilanes catalyzed by $FeCl_3$

The photophysical properties of oligomer were briefly examined. The oligomer exhibits fluoresecsence in the purple region with high quantum yields in CH_2Cl_2 and EtOAc. The emission spectrum in the solvents shows vibronic fine structure. Importantly, this oligomer bears a long chain aliphatic moiety which increases the solubility for the convenience of processing leading to devices for optoelectronic investigations. Synthesis of analogous oligomers by the $FeCl_3$-catalyzed substitution/cyclization sequential process and their potential optoelectronic applications are currently going on in our laboratory.

Keywords: Propargylic Alcohols, Iron Trichloride, Nucleophilic Substitution; γ-alkynyl ketone, enoxysilane; optoelectronic, oligomer